Remarks

Claims 1-52 are pending. Claims 1-25, 34, and 36-52 are cancelled. Claims 26, 29 to 33 and 35 are amended. Claims 53-73 are added. Applicants submit that the election of claims in response to the above described Restriction Requirement are made with traverse. Applicants wish to thank the Examiner for the Examiner's conversation with Applicants' representative pertaining to Applicants submissions set forth herein.

In response to the Restriction Requirement dated September 29, 2002, Applicants elect **Group** VIII, **Claims** 26-33, and 35 for prosecution on the merits, with traverse. The Restriction Requirement requires that Applicants elect either a method wherein the step of contacting is performed *in vitro* or *in vivo* as recited in claims 27 and 28, respectively. Applicants elect contacting ***in vivo***. The Restriction Requirement also stipulates that Applicants must elect a type of compound from claims 29-30 or 32-33. Applicants submit that they have narrowed the scope of independent claims 26, 31 and 35 to recite "an inhibitor". Support for this amendment may be found on pages 67 to 75 of the specification. Thus, the invention of amended claims 26, 31 and 35 now defines the term "compound" by its **physical property** i.e. "an inhibitor". Applicants believe that this amendment provides a precise definition of the compounds encompassed by the claims and narrows the claims sufficiently to obviate the Examiner's requirement for election of a particular type of compound. Indeed, the Applicants respectively point out to the Examiner that the essence of the invention does not lie in any specific type of compounds that could be used to carry out the claimed method (e.g. a polypeptide, a small chemical molecule, an antisenses polynucleotide), but it lies in the inhibition of the DnaI pathway. Accordingly, Applicants have not selected a compound from those of claims 29-30 or 32-33. In the event that the Examiner finds this election to be unresponsive, Applicants request that they be given the opportunity to discuss the Restriction Requirement with the Examiner by telephone at the Examiner's convenience.

Rejoinder of Nucleic Acid and Amino Acid Claims

As indicated in the Restriction Requirement, the Examiner has required that Applicants elect an invention selected from groups VIII or IX as they pertain to methods of inhibiting bacteria or treating a bacterial infection in an animal comprising contacting the bacteria with a

compound or administering to the animal a compound that is active on (1) a polypeptide or (2) on a gene encoding the polypeptide comprising SEQ ID NO: 16. Applicants submit that these two restricted groups should be examined together.

Applicants submit that the claims of the invention recite a method for inhibiting a bacterium comprising contacting the bacterium "with an inhibitor **active on** a polypeptide comprising the amino acid sequence of SEQ ID NO: 16 or a gene encoding said polypeptide". Applicants submit that the phrase "active on" is defined in the specification at page 17 as referring to a compound which is active on a particular target wherein the target "is an important part of a *cellular pathway* which includes that target and that an agent or compound acts on that pathway...the agent or compound may act on a component *upstream or downstream* of the stated target". The claims of the present invention relate to a method of inhibiting a bacterium by contacting the bacterium with an inhibitor which is active on a polypeptide or a polynucleotide molecule encoding the polypeptide; that is, an inhibitor which is active on a pathway which begins with the gene sequence and ends with the functional polypeptide. The recitation of the phrase "active on" in the claims therefore encompasses inhibitors that act both at the polypeptide level and at the gene level. Accordingly, Applicants submit that the restriction set forth by the Examiner is improper, in that, according to the specification, the inhibitor recited in the elected claims encompasses compounds which are active on a cellular pathway; a cellular pathway which necessarily includes both polypeptide activity and gene expression. Applicants therefore request that the restriction of groups VIII and IX be withdrawn, and the two groups be examined together, as both groups fall under the recitation it the claims of "active on".

Rejoinder of *in vivo* and *in vitro* Claims

The Examiner has required election of claims that relate to the elected methods performed either *in vitro* or *in vivo*. Applicants request reconsideration. Applicants submit that the elected base claim relates to a method of "contacting" a bacterium with a compound. The recited "contacting" step necessarily encompasses both *in vitro* and *in vivo* contacting steps. It also encompasses contacting steps that could be considered being neither *in vitro* nor *in vivo* such as contacting steps carried out in industrial applications (e.g. sanitization, disinfection, etc). The method of the invention relies, in part, on the novel discovery that compounds which inhibit

the S. aureus DnaI molecule at the gene and/or protein level are able to inhibit *S. aureus* growth and replication. Thus, the Examiner's search for prior art that would relate to *contacting* a bacterium with a compound which inhibits DnaI would necessarily encompass art which teaches *in vitro* and *in vivo* contacting steps. Accordingly, Applicants submit that the search for *in vitro* and *in vivo* methodologies would be co-extensive, and would therefore not place any undue search burden on the Examiner.

Species Election

As discussed with the Examiner, Applicants respectfully request that if the arguments set forth upon above are not found to be persuasive, that the Examiner would consider converting the restriction of gene/polypeptide, *in vitro/in vivo*, and the compound restriction from a restriction of distinct inventions to species of the base invention of inhibiting a bacterium or treating a bacterial infection by contacting a bacterium with a compound which inhibits DnaI. Applicants request that the Examiner reconsider the restriction of inhibition of DnaI gene or polypeptide to be species of "inhibition of DnaI", and likewise request that the Examiner consider the restriction of contacting *in vitro* and *in vivo* to be species of "contacting", and that the compounds of elected claims 29-30 and 32-33 be considered as species of the genus "inhibitor" as recited in amended claims 26, 31 and 35. Such species restriction would not place any *undue* examination burden on the Examiner, but would only require that if the elected species were to be found allowable, the Examiner would examine the non-elected species. With respect to the suggested species of "inhibitor", Applicants submit that the claims as amended are characterized by a **physical property** which significantly narrows the search burden on the Examiner; that is, the Examiner need only search for *inhibitors* which reduce DnaI activity or expression. Applicants submit that, in view of the present invention as a novel and important step in the combat against drug resistant S. aureus infection, Applicants should be able to reap the full benefit if their discovery through at least the examination of the full scope of the present claims. Applicants accordingly request that, at the least, the restriction of the present claims into the groups of DnaI gene/polypeptide and *in vivo/in vitro* be withdrawn and made a species election.

New Claims

Applicants submit new claims 53-73 that relate to methods for inhibiting a bacterium (analogous to elected claims 26-30) and methods for treating or preventing a bacterial infection (analogous to elected claims 31-33, and 35). The recitation of "*inhibitor*" or "*antibacterial agent*" may be found on pages 17, 61-78 and 36, 68, respectively, of the specification. Specifically, new claims 53-58 are supported by pending claims 27-30. The recitation of "*decreasing the activity*" or "*decreasing the expression*" in the newly added claims may be found on page 34 and 44, respectively, of the specification. With respect to newly added claim 59 and 66, support for the recited % identity, % similarity, and size and fragment may be found at pates 49-51 of the specification, as well as in the currently pending claims. The recitation of the specific activity of the recited DnaI polypeptides is found throughout the specification and also in the issued parent patent application (of which the present application is a CIP), now U.S. Patent No. 6,376,652. The support for new claims 60-64 may be found in the currently pending claims 27-30 as well as throughout the specification. The support for newly added claim 65 may be found in the currently pending claim 31, as well as page 8 of the specification. Support for newly added claims 67 and 68 may be found at page 18, as well as pages 68-75 of the specification. New claim 69 is supported by the teachings in the specification at page 36, second paragraph. Support for claims 70 and 71 is found throughout the specification and also in the issued parent patent application (of which the present application is a CIP), now U.S. Patent No. 6,376,652. Lastly, support for new claims 72-73 is found at least at page 38, fourth paragraph of the specification.

As for the elected claims, new claims 53-73 are restricted to compounds which are define as being "an inhibitor" or "an antibacterial agent". Applicants submit that, similar to the preceding discussion relating to the term "compound", the new claims encompass only a limited number of compounds which are precisely defined by their **physical property**. Accordingly, Applicants submit that the new claims provide a precise definition of the compounds encompassed by the claims and that these claims are sufficiently narrow to allow the Examiner to search for prior art without an election of a particular type of compound.

Applicants further submit that, similar to the preceding discussion relating to the co-

extensive examination of the gene/polypeptide aspects of the currently pending claims, the recitation in the newly added claims of an inhibitor "capable of decreasing the activity of or decreasing the expression of a polypeptide" should be examined as a single invention and not restricted into gene/polypeptide elements. Applicants submit that the specification defines a "decrease in activity" as a "reduced level of measurable activity of a polypeptide" (p. 34, lines 19-21). Such a decrease in activity, as defined by the specification, would therefore encompass a decrease in the activity of the polypeptide itself, or a decrease in expression of the polypeptide, which would inherently result in a decrease in protein activity. Therefore applicants submit that the recitation in the new claims of "decreasing the activity" encompasses both polypeptide activity as well as gene expression and, thus, these elements should be examined together.

Applicants also submit that the sequences of SEQ ID Nos. 2, 16, and 18 in the newly added claims should be examined together because the search would be co-extensive, and the sequences overlap significantly. SEQ ID NO: 2 is the full-length DnaI sequence useful in the invention and this sequence has already been found patentable in parent application, now U.S. Patent No. 6,376,652. SEQ ID Nos 18 and 16 are proteolytic fragments of SEQ ID NO: 2: SEQ ID NO: 18 is amino acid residues 64-313 of SEQ ID NO: 2; SEQ ID NO: 16 is amino acid residues 150-313 of SEQ ID NO: 2. Accordingly, where the newly added claims recite the polypeptides *comprising* the sequence of SEQ ID Nos 2, 16, or 18, a search of a polypeptide comprising SEQ ID NO: 2 will necessarily encompass a search of polypeptides comprising SEQ ID Nos 16 and 18. Thus, all the Examiner need search is the sequence of SEQ ID NO: 2, a sequence which has already been searched and found patentable in the parent application. Applicants submit that this does not place any undue search burden on the Examiner, and respectfully request that the newly added claims be examined for the plurality of sequences recited therein.

Lastly, Applicants submit that, as discussed above, the examination of *in vitro* and *in vivo* "contacting" steps recited in claim 54-56 and 60-62 should be examined concurrently. The recited step of "contacting" encompasses both *in vitro* and *in vivo* contacting steps. The method of the invention relies, in part, on the novel discovery that compounds that inhibit the S. aureus DnaI molecule at the gene and/or protein level are able to inhibit S. aureus infection. Thus, the Examiner's search for prior art that would relate to *contacting* a bacterium with a compound that

inhibits DnaI would necessarily encompass art that teaches *in vitro* and *in vivo* contacting steps. Accordingly, Applicants submit that the search for *in vitro* and *in vivo* methodologies would be co-extensive, and would therefore not place any undue search burden on the Examiner.

To the extent that the Examiner requires restriction of the newly added claims, similar to the restriction set forth in the present Restriction Requirement, Applicants elect methods comprising "decreasing the activity"; and contacting *in vivo*.

This Response is being filed within 30 days from the Restriction Requirement mailed September 29, 2003 and no fee is believed to be due. However, should any fees be required to ensure consideration of this response, the Commissioner is authorized to charge Deposit Account 16-0085, Reference No. 21715/1010.

Respectfully submitted,

Date: October 29, 2003

Name: Kathleen M. Williams
Registration No.: 34,380
Customer No.: 29933
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel: 617-239-0100